

Solar urticaria successfully treated with intravenous immunoglobulin

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Summary

Idiopathic solar urticaria (SU) is a rare, debilitating photodermatosis, which may be difficult to treat. First-line treatment with antihistamines is effective in mild cases, but remission after phototherapeutic induction of tolerance is often short-lived. Other treatment options include plasma exchange, photopheresis and ciclosporin. We present two cases of severe, idiopathic SU, which were resistant to conventional treatment. Both patients achieved remission after administration of intravenous immunoglobulin (IVIg) and have remained in remission at 13 months and 4 years, respectively. There are only two case reports of successful treatment of solar urticaria with IVIg. In our experience IVIg given at a total dose of 2 g/kg over several 5-day courses about a month apart is an effective treatment option for severe idiopathic SU. It is also generally safe, even if certainly subject to significant theoretical risks, such as induction of viral infection or anaphylaxis.

Solar urticaria (SU) is an uncommon photodermatosis, classified as either primary idiopathic or secondary SU. Secondary SU occurs after exogenous photosensitization or due to conditions such as porphyria and lupus erythematosus.¹ The incidence of primary SU is unknown. It is suggested to account for 0.04% of all cases of urticaria.² There is a female preponderance and it usually occurs between 10 and 50 years of age.² Typically, an itching or burning sensation with associated erythema occurs within 5–10 min of sunlight exposure, followed by wealing papules or plaques. Most commonly, patients develop the rash after exposure to ultraviolet (UV)A (320–400 nm), or visible light (400–600 nm). UVB (280–320 nm) and infrared light (> 600 nm)³ are less commonly responsible.

Idiopathic SU may be difficult to treat. Efficacy of treatment depends on the patient's action spectrum and disease severity, as expressed by the minimum urticarial dose (MUD). We present two patients with severe idiopathic SU who were successfully treated with

intravenous immunoglobulin (IVIg) and were still in remission up to 4 years after treatment.

Report

Patient 1 was a 38-year-old woman, who presented in winter with a 1-month history of an intensely pruritic, papular, erythematous rash. The rash was limited to sun-exposed areas, appeared within minutes of light exposure, and resolved within several hours. There was associated nausea, marked tingling in the affected skin and several presyncopal episodes during evolution of the rash. There was no contributory medical history and she was taking no medication. The patient's full blood count, urea and electrolytes and liver function tests were normal. Results of an autoantibody screen, including antinuclear antibodies (ANA), extractable nuclear antigens (ENA), anticardiolipin and anti-double-stranded (anti-ds)DNA antibodies, and a porphyrin screen, were all negative. SU was diagnosed clinically and the patient was referred for monochromator and solar simulator phototesting. This revealed wealing to UVB, UVA1 and UVA2 in addition to strong reactions to visible light. Solar simulator responses showed wealing to minimal UV exposure, confirming the diagnosis of severe SU. The patient also had persistent reactions at 24 h with an minimal erythema dose (MED)

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of 20 mJ/cm² at 300 nm, 1 J/cm² at 320 nm and 5 J/cm² at 370 nm, suggesting a coexisting polymorphic light eruption (PLE) tendency. Induction of tolerance was attempted with whole-body UVA treatment according to the UV rush hardening regimen.⁴ The patient received two identical courses, starting at 0.1 J/cm² and reaching a maximum dose of 10.00 J/cm². This was unsuccessful. Bath 8-methoxypsoralen UVA (PUVA), was started next and 18 treatments were completed, reaching a maximum dose of 0.60 J/cm². This was ineffective. UV treatment was stopped and ciclosporin 3 mg/kg/day started. Improvement was noted and the dose was increased to 4 mg/kg/day; however a UVA challenge with 1 J/cm² resulted in acute urticaria. The dose of ciclosporin was increased to 5 mg/kg but the patient remained symptomatic despite minimum sunlight exposure and total sunscreen. Finally, the patient was started on intravenous immunoglobulin (IVIg) 0.4 g/kg/day over 5 days and ciclosporin was discontinued. The patient reported an improvement in symptoms after two courses. After six courses, administered at 1-month intervals, full remission was achieved. A repeat UVA challenge with 15 J/cm² elicited no response. IVIg treatment was stopped and the patient was still in remission after 13 months of follow-up.

Patient 2 was a 33-year-old woman, who presented in spring with an 8-month history of a recurrent rash. The rash was confined to sun-exposed areas, occurred within seconds of exposure to sunlight (including through glass) and resolved within 1–2 h. It was intensely pruritic with a sensation of burning in the affected skin. On several occasions there was associated dyspnoea and headache. The patient also had a history of PLE, allergic rhinitis and asthma, and there was a family history of systemic lupus erythematosus. The patient had been taking no medications before the onset of this condition. Results of routine blood tests were normal. An autoantibody screen revealed a mildly elevated ANA (1 : 100), and results for ENA, anti-cardiolipin and anti-dsDNA antibodies were negative. A diagnosis of SU was made and the patient was referred for monochromator and solar simulator phototesting. Solar simulator testing revealed extreme sensitivity, confirming the diagnosis. The patient also had an MED of 40 mJ/cm² at 300 nm, 0.25 mJ/cm² at 320 nm, 1.3 mJ/cm² at 370 nm and no reaction at 400 nm. A combination of high-dose antihistamines and leukotriene antagonists was unhelpful. Oral steroids, which the patient had previously, received from her general practitioner, had also been ineffective. A rush desensitization programme⁴ was started at a dose of

0.25 J/cm² and increased to 1.11 J/cm² over a 4-week period. This resulted in a brief remission. Unfortunately, daily attendance at the hospital was inconvenient for the patient, and treatment was changed to twice-weekly whole-body PUVA. The patient's symptoms returned within weeks and repeat MED tests confirmed reactivity at very low levels of exposure, as did a positive response to autologous serum irradiated at 10 J/cm² UVA for 20 min. IVIg 0.4 g/kg/day over a 5-day period was started. After the first course the patient reported mild symptom improvement. After the second course she was able to tolerate 15 min of sun exposure without signs or symptoms and, was no longer reactive to sunlight exposure through glass. She also reported resolution of her PLE. After three courses given at 4-week intervals, the patient was able to tolerate 30 min of summer sunshine without sunscreen, thus treatment was stopped. The patient was still symptom-free after > 4 years of follow-up, no longer required antihistamines and had not experienced any further episodes of PLE.

The epidemiology of idiopathic SU is unknown. In mild cases, first-line treatment with H1-blocking antihistamines may be sufficient. Induction of tolerance with an artificial UV source is recommended in more severe cases. Treatment is based on the observation that areas of UV-exposed skin are less likely to react than skin which is habitually covered and that areas which have recently reacted to light exposure may not react to subsequent exposure for a period of time.² Remission after phototherapeutic induction of tolerance is frequently short-lived and patients typically require maintenance treatments. Photochemotherapy may offer a longer remission.⁵

Edstrom *et al.*⁶ successfully treated a case of SU with ciclosporin but the condition relapsed within 2 weeks. Individual case reports exist of the effectiveness of plasma exchange⁷ and photopheresis.⁸ There are only two case reports of successful treatment of SU with IVIg in the literature.^{9,10} In one case,⁹ IVIg was administered in combination with PUVA.

The exact mechanism of action of IVIg is not understood. It is suggested that it may block the Fc portion of IgG molecules on reticuloendothelial cells and is thought to have a direct inhibitory effect on B-cell and/or T-cell function. In SU, IVIg may provide anti-idiotypic antibodies capable of suppressing histamine releasing autoantibodies. IVIg is a manufactured blood product, derived from human serum. Despite screening donors for infectious agents, the presence of currently unidentified agents does raised some concern. The cost of the drug is also a consideration, at an average price of €50/g. Adverse

effects with IVIg are usually rare and self-limiting. Anaphylaxis in IgA-deficient people and cases of arterial and venous thrombosis have been described.

We present two cases of severe idiopathic SU resistant to conventional treatment. Both achieved remission after administration of IVIg and have remained in remission after 13 months and 4 years, respectively. In our experience IVIg is an effective treatment option for severe SU. It is also safe, even if certainly subject to certain theoretical risks, such as introducing viral infection or anaphylaxis.

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